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EXAMINER
DUBROLE, C

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 10/4/93 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 2-5, 7-10 & 18-47 are pending in the application.
   Of the above, claims 2-5, 7-10 & 20-46 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 18, 19 & 47 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 2-5, 7-10 & 18-47 are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. Upon reviewing this application, the Examiner has determined that substantial new grounds of rejection will be applied. Thus, prosecution of this application will resume. This Office action will therefore be NON-FINAL.

16. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

17. Claims 18, 19 and 47 are rejected under 35 U.S.C. § 101 because the invention as disclosed is inoperative and therefore lacks utility.

18. Claims 18, 19 and 47 are drawn to vaccines and their use, and claim 19 is explicitly drawn to the use of such vaccines in humans.

19. Vaccines are defined in Webster's New World Dictionary, 3rd College Edition, as "any preparation of killed microorganisms, living weakened microorganisms, etc. introduced into the body to produce immunity to a specific disease by causing the formation of antibodies"

20. That the UTAA is useful as a vaccine is unbelievable on its face, because many reasons exist to doubt the objective truth of such a utility. These reasons include those outlined by Urban et al, 1992 at page 634, namely "Even if immunogenic epitopes are provided, immune surveillance may not be effective for a variety of reasons. first, the carcinogen may suppress the immune system. Second, most cancers arise in cells that are not 'professional' antigen-presenting cells (APCs), and in the absence of infiltrating APCs, such tumors may not produce sufficient amounts of critical costimulatory factors to activate responding CTLs. In fact, antigen expression in the absence of costimulatory factors may tolerize T cells to the tumor-specific molecule(s). Third, immunogenic T-cell epitopes may be provided, but they may be subdominant, cryptic, or otherwise weakly antigenic....Finally, even if the host can be immunized against the tumor-specific protein, such cells may not exert their effects their effects within the tumor because of a local environment that prevents terminal T-cell differentiation."

21. While Urban et al fail to rule out the possibility of using tumor antigens as therapeutics, it is clear that their review of the relevant literature at the time (1992) led them to conclude that "synthetically derived immunogenic peptides in appropriate adjuvants **may possibly be developed**", (emphasis added) page 636.

22. Applicants are claiming a vaccine containing a specific protein (UTAA) which protein appears to possess diagnostic value, however no data have been provided showing that the protein is in any way useful as a vaccine component, let alone teaching which peptides derived from the protein might be useful. In fact, the presence of antibodies to UTAA in cancer patients underscores the unbelievability of the asserted utility, since these antibodies appear not to be able to protect the patients.

23. Furthermore, it is known that MHC Class expression is reduced in tumor cells, thus they are able to evade eradication by the immune system (see for example Hammerling et al, 1987). Hence, it appears unlikely that any vaccine which does not take into account the reduced expression of MHC, and therefore the reduced presentation of tumor antigen for cytotoxic T-cells, will fail to function as a *vaccine*.

24. As set forth in In re Langer, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope. Assuming that sufficient reason to question the statement of utility and its scope does exist, a rejection for lack of utility under §101 will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the statement of utility and its scope as found in the specification are true. Cf. In re Marzocchi, 58 CCPA 1069, 1073, 439 F.2d 220, 223, 169 USPQ 367, 369 (1971)(involving the enablement requirement of 35 U.S.C. §112, first paragraph). (emphasis in original)

25. The MPEP 608.01(p) states "Utility must be definite and in currently available form; (Brenner v. Manson, 383 U.S. 519, 148 USPQ 689) not merely for further investigation or research but commercial availability is not necessary. Mere assertions such as `therapeutic agents,' (In re Lorenz et al., 49 CCPA 1227, 305 F.2d 875, 134 USPQ 312; cf. Ex parte Brockmann et al., 127 USPQ 57) `for pharmaceutical purposes,' (In re Diedrich, 50 CCPA 1355, 318 F.2d 946, 138 USPQ 128) `biological activity,' (In re Kirk et al., 54 CCPA 1119, 153 USPQ 48; Ex parte Lanham, 135 USPQ 106) `intermediate,' (In re Joly et al., 54 CCPA 1159, 153 USPQ 45; In re Kirk et al., 54 CCPA 1119; 153 USPQ 48) and for making further unspecified preparations are regarded as insufficient."

"..incredible statements..or statements deemed unlikely to be correct by one skilled in the art..in view of the contemporary knowledge in the art will require adequate proof on the part of applicants for patents. More particularly, if the utility relied on is directed solely to the treatment of humans, evidence of utility, if required, must generally be clinical evidence.." the MPEP goes on to say "..a drug which is not sufficiently safe under the conditions of use for which it is said to be effective will not satisfy the utility requirement..".

26. As pointed out in Brenner v Manson, 148 USPQ 689,:

> "This is not to say that we mean to disparage the importance of contributions to the fund of scientific information short of the invention os something 'useful,' or that we are blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. '(A) patent system must be related to the world of commerce rather than to the realm of philosophy.'"

27. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

28. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

29. The specification fails to teach the administration of any vaccine which inhibits cancer in the recipient. As discussed above, it does not appear that the vaccine in fact "works", hence the specification has not taught how to use the vaccine.

30. While the specification does teach the administration of a composition which increases antibody titer to UTAA, there are no teachings that this titer increase is indicative of cancer inhibition in vivo.

31. Applicants have relied upon page 17, lines 5-13 of the specification for teaching of inhibition of cancer. The teaching appears to be speculative and is not considered sufficient to meet the enablement requirement.

32. The specification fails to teach a vaccine containing the composition of claim 18 or 47. Nowhere does the specification teach immunization with substantially purified material, as discussed above.

33. Claims 18, 19 and 47 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

34. Claims 18, 19 and 47 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

35. Applicants appear to be using the term "vaccine" in a manner which is repugnant to the art. Thus, it appears that the term "vaccine", while well known to skilled artisan working in the field, is not adequately defined in the specification for its contextual instant meaning. For example, Applicants argue in the Brief that "none of the claims require cancer 'inhibition'", and that "because claims 18 and 47 concern a vaccine *per se*, the utility of these claims is satisfied by any utility, including the preparation of diagnostic antibodies", appeal brief, page 8.

36. The Examiner would argue that the term "vaccine" connotates that defined by Webster's above. Clearly then, vaccines are not used to raise antibodies useful for diagnosis, but are used to confer protection from an infectious agent. Applicants should either abandon the "vaccine" language, or make clear for the record what they consider the term "vaccine" to mean.

37. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

38. Claims 18, 19 and 47 are rejected under 35 U.S.C. § 102(b) as being anticipated by R.K. Gupta et al, 1987 abstract.

39. Gupta et al teach the vaccination of melanoma patients with tumor cells, at least one of which (M14 cells) expresses melanoma tumor associated antigen. It seems likely that the cell line also produces UTAA in light of the disclosure of Gupta et al, 1984 abstract. Applicants disclosure supports this assertion (p53-54).

40. Since the claimed vaccine composition merely "comprises" the UTAA antigen, the M14 vaccine anticipates the claims, as the claim language fails to exclude the entire cell. Worth noting is the fact that Applicants have defined "purified" to mean that the antigen is merely purified over that found in nature (page 5 of Applicants brief), and that "substantially purified" means approximate 100-fold purified over nature (page 6 of the brief). Certainly the M14 cells comprise less than 1% of the source in nature from which they were derived (a human being), thus these cells in fact comprise "substantially purified" UTAA, using Applicants' terminology.

41. Claims 18 and 47 are rejected under 35 U.S.C. § 102(b) as being anticipated by Francisco X. Real et al, U.S. Patent 4,562,160.

42. Real et al teach the purification of a 90kD glycoprotein tumor antigen. They teach that the antigen is useful to generate monoclonal antibodies for diagnosis (see column 5). It is unclear if this is the same antigen being claimed in claims 18 and 47 of the instant application.

43. Applicants arguments are somewhat confusing. Applicants have mainly argued by describing their invention, as opposed to identifying the differences between the protein of the prior art and the protein of the invention. Applicants have however argued that the IEP's are different for the 2 proteins, but only by 1/2 of a pH unit.

44. As Applicants themselves have pointed out in the specification, the UTAA is not restricted to urine, but is expressed on tumor cells as well. The difference in isoelectric points reported is well within experimental error, and it is the Examiner's position that the burden has been shifted to Applicants show that the protein of Real et al does not anticipate the instantly claimed protein.

45. This reference was not applied against Applicants' vaccine claims previously, because Real et al do not use their antigen in a vaccine (in the conventional sense of the word "vaccine"), however in view of the unusual and repugnant meaning applicants have assigned the word "vaccine", i.e. that vaccines can be useful to develop diagnostic antibodies, this reference is deemed to anticipate the instant claims. The FD antigen, when injected into mice to develop monoclonal antibodies as taught by Real et al would in fact constitute a "vaccine" using Applicants' parlance.

46. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989).

The CM-1 Fax Center number is (703) 305-3014

47. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Chris Dubrule whose telephone number is (703) 308-0708. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CJD

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